

EXHIBIT 2

AUSTRALIA

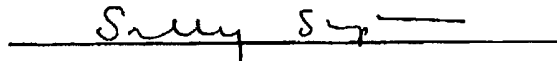
Patents Act 1990

IN THE MATTER OF  
US Patent Application No. 09/446,109  
by The University of Queensland

EXHIBIT VBS-2

This is Exhibit VBS-2 referred to in the Statutory Declaration by Vivien Bedford Santer  
dated 13<sup>th</sup> May, 2004

Before me:



SALLY ANN SHRIMPTON  
3rd Floor, 509 St. Kilda Rd, Melbourne 3004  
A current practitioner within the meaning  
of the Legal Practice Act 1996.

A person empowered to witness Statutory  
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1: Semin Arthritis Rheum. 1983 Nov;13(2):160-8.

Related Articles, Links

# Carrageenin-induced arthritis: V. A morphologic study of the development of inflammation in acute arthritis.

Santer V, Sriratana A, Lowther DA.

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Following a single injection of the polysaccharide carrageenin into the rabbit knee joint, a rapid inflammatory process occurs in the joint space and synovial membrane, followed by changes in the articular cartilage. Initially there is an influx of cells, mainly PMNs, into the synovial fluid, accompanied by proliferation of the synovial lining cells and infiltration of the synovial membrane. The numbers of synovial fluid cells decline gradually after 24 hr. The reaction in the synovial membrane is greatest at day 7, and inflammation is still evident at day 21. Initially, the infiltrate consists mainly of PMNs, but by day 7 it is predominantly mononuclear, with small clusters of lymphocytes. The articular cartilage shows loss of metachromasia with toluidine blue at 3-14 days after injection, but stains normally after day 21. Electron microscopy shows damage to the chondrocytes at day 1 and 7, with complete destruction of cells in the surface layer. At day 7 cells in the deeper layers have lost the apparatus required for proteoglycan synthesis, but at day 21 the cells appear virtually normal. There was no evidence for a direct inhibitory effect of carrageenin on proteoglycan biosynthesis. Most labeled carrageenin was rapidly cleared from the joint space, but about 10% was retained in the synovial membrane and 0.6% in articular cartilage at 48 hr after injection. Since the increase and decline in PMN numbers respectively precede the cartilage damage and recovery, it is suggested that there may be a correlation between the clinical activity of arthritis and the number of PMNs in the synovial fluid.

PMID: 6673111 [PubMed - indexed for MEDLINE]

☐ 3: Arthritis Rheum. 1977 Apr;20(3):834-40.

Related Articles, Links

**Carrageenin-induced arthritis. IV. Rate changes in cartilage matrix proteoglycan synthesis.**

**Carmichael DJ, Gillard GC, Lowther DA, Handley CJ, Santer VB.**

A localized inflammatory response was initiated by both single and repeated injections of carrageenin into femorotibial joints. Histologic changes were observed 24 hours after a single intraarticular injection, and an inhibition in the in vitro rate of proteoglycan synthesis was detected 72 hours after the injection. This inhibition was relieved in vitro by the addition of beta-D-xyloside, an exogenous initiator of glycosaminoglycan biosynthesis. Following repeated carrageenin injections, most cells appeared to be dead on histologic examination and no in vitro proteoglycan synthesis could be detected; nor could any stimulation be achieved by adding xyloside.

PMID: 856216 [PubMed - indexed for MEDLINE]